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Authors

Bostwick, A Doran
Jones, Barbara E
Paine, Robert
et al.

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Potential Impact of HAP Guidelines on Empiric Antibiotics: An Evaluation of 113 VA Medical Centers

Authors:
A Doran Bostwick
Division of Pulmonary & Critical Care Medicine. SLC VA Health System and University of Utah
anne.bostwick@hsc.utah.edu
30N 1900 E 70 1 Wintrobe
Salt Lake City, UT 84132
254-723-6944
Barbara E Jones, MD, MSc. Division of Pulmonary & Critical Care Medicine. SLC VA Health System and University of Utah
Robert Paine, MD. Division of Pulmonary & Critical Care Medicine. University of Utah
Matthew Bidwell Goetz, MD. Infectious Diseases Section. VA Greater Los Angeles Healthcare System and David Geffen School of Medicine at UCLA
Matthew Samore, MD. Division of Epidemiology, Salt Lake City VA Health System and University of Utah.
Makoto Jones, MD, MSc. Division of Epidemiology and Infectious Disease, Salt Lake City VA Health System and University of Utah.

AD Bostwick had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Additional author contributions are: B. Jones data collection/management, study design, manuscript preparation; R.Paine, study design, manuscript preparation; M. Goetz, manuscript preparation; M. Samore, manuscript preparation; M Jones, data collection/management, study design, manuscript preparation.

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ABSTRACT

Rationale: The 2016 guidelines for hospital-acquired pneumonia (HAP) suggest applying a universal antibiogram resistance threshold in addition to patient criteria to determine empiric coverage. The impact of these recommendations is unknown.

Objectives: 1) Describe national antibiotic use and microbiology patterns for HAP among patients with non-infectious admissions, 2) measure the predictive performance of the antibiogram threshold and risk factors, and 3) estimate the change in practice with guideline implementation.

Methods: We conducted a retrospective analysis of all hospitalizations without initial infection but with secondary pneumonia diagnoses at Veterans Affairs Medical Centers between 10/1/2012 and 9/30/2015. For each hospitalization we extracted: presence of MRSA and resistant GNR (R-GNR) in cultures, anti-MRSA and anti-pseudomonal antimicrobial administration, and facility-level prevalence of MRSA and R-GNR. We calculated the percent hospitalizations with resistant organisms, broad-spectrum antibiotics, and the predictive performance of patient characteristics and prevalence thresholds for MRSA.

Measurements and Main Results: Among 3,562 cases, 5.17% were positive for MRSA and 2.30% for R-GNR. The recommended MRSA prevalence threshold was 100.00% sensitive (95% confidence interval[CI], 98.02–100.00%) and 0.03% specific (95% CI,0.00–0.16%) for MRSA-positive culture, leading to overtreatment of 94.81%

(95% CI,94.02-95.50%) of patients. Pressor order (odds ratio[OR] 3.89; 95% CI,1.17–12.91) and IV antibiotics within the past 90 days (OR,1.98; 95% CI,1.03–3.81) were associated with MRSA. Mechanical ventilation was associated with R-GNR (OR,4.37; 95% CI,1.52–12.57).

Conclusions: The guideline-recommended antibiogram threshold and characteristics did not improve prediction of MRSA or R-GNR and would have led to an increase in MRSA treatment.

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INTRODUCTION

Hospital-acquired pneumonia (HAP) is a common nosocomial infection with high mortality and an association with resistant bacteria.(1-6) Antimicrobial therapy, including empiric therapy with activity against resistant organisms, should be tailored to individual patients, but the magnitude of risk for resistant infections is largely unknown.(6-13) Recent guidelines from the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) for the diagnosis and management of HAP provide recommendations for empiric antimicrobial selection based on perceived risk factors for resistant infections. They strongly recommend that each hospital generate antibiograms and provide thresholds for the proportion of resistance that would indicate need for coverage of methicillin-resistant *Staphylococcus aureus* (MRSA). Specifically, for HAP, coverage for MRSA is recommended if prevalence of resistance is >20% or unknown.(4, 14) MRSA coverage and 2 anti-pseudomonals are also recommended if the patient has

received prior intravenous antibiotics in the preceding 90 days, is in shock or requires ventilatory support. These guidelines were intended to “minimize patient harm and exposure to unnecessary antibiotics and reduce the development of antibiotic resistance”.(4) However, the implications of these guidelines for antibiotic use are unknown, as is the prevalence of resistance nationally.

Using a large national database we sought to 1) describe existing national practice and microbiology patterns prior to the guidelines, including the frequency of initial treatment for multi-drug resistant organisms and culture methods for HAP; 2) measure the predictive performance of the specified risk factors and antibiogram resistance threshold to identify patients with resistant organisms; and 3) estimate the change in practice with guideline implementation.

METHODS

Setting and Subject Selection

We conducted a retrospective analysis of HAP across all Veterans Affairs Medical Centers (VAMCs). We included all patients admitted between October 1, 2012 and September 30, 2015 admitted to acute-care medical or surgical wards, an observation unit, or an intensive care unit, with a non-principal diagnosis of pneumonia by ICD-9 (481- 486). We ended our sample period in 2015 to avoid the effect of change between ICD-9-CM and ICD-10-CM. We then limited our sample to non-infectious admissions by excluding those with a principal diagnosis of pneumonia, respiratory distress, or sepsis (507.0, 518.81, 518.84, 799.1, 785.52, 995.91, 995.92) and those who received antibiotics or cultures within the first 48 hours in order to improve our ability to specifically identify HAP (Figure 1). These were excluded because although HAP can occur after an infection present on

admission, retaining these admissions could lead to frequent misclassification of community-acquired pneumonia as HAP. Timing of infection was defined as the date of earliest cultures or antibiotics. We validated the precision of our approach through chart review of 100 charts.

In an effort to ensure the internal validity of our study, we initially limited our cohort of HAP patients to those who did not receive antibiotics or cultures during the first 48 hours of admission. To explore the generalizability of our findings we subsequently completed a sensitivity analysis among all patients with a secondary diagnosis of pneumonia including those who received antibiotics or cultures in the initial 48 hours (Figure 1).

Data was accessed and analyzed using Veterans Informatics and Computing Infrastructure (VINCI).(15)

Patient-level Measurements

After identifying our cohort of HAP patients, we then evaluated the following patient characteristics: age, sex, admission service, ICU admission, orders for vasopressors, average length of stay, thirty-day mortality, and presence of comorbid disease, including: cerebrovascular disease, congestive heart failure, diabetes, renal disease, and neoplastic disease. Next, we measured the percent of HAP patients who received empiric antimicrobial agents with activity against MRSA and two-drug therapy for resistant Gram-negative rods (R-GNR) as recommended in the 2016 ATS/IDSA guidelines for HAP.(4) For MRSA the suggested agents were: vancomycin and linezolid. For R-GNR the suggested agents were: piperacillin-tazobactam, cefepime, ceftazidime, imipenem, meropenem, aztreonam, ciprofloxacin, levofloxacin, amikacin, gentamicin, tobramycin, colistin, and

polymyxin B. Of note, Veteran Affairs pharmacy benefits management leaves all decisions regarding which antibiotics to carry to the local hospital or station. They state that these decisions should be based on local culture and sensitivity patterns. Additionally, we focused on the number of anti-pseudomonals being used to evaluate concern for resistance by the provider in an effort to accommodate prescribing practices. We also measured the percent hospitalizations that had blood and respiratory cultures obtained at time of treatment. We measured the percent of hospitalizations in which cultures detected MRSA and GNR resistant to piperacillin-tazobactam. Nasal MRSA PCR screening data were not included in the estimates of resistance prevalence.

Antibiogram Development Feasibility and Application to HAP Cohort

We extracted all inpatient culture data from all VAMCs between 2011 and 2014 to determine the ability of hospitals to generate antibiograms by location (hospital-wide vs ICU) and culture type (respiratory vs all). We defined a hospital's ability to generate an antibiogram as the presence of ≥ 30 cultures during the year prior to the pneumonia.(16) For each facility we measured the ability to develop the following antibiograms in 2014: hospital wide *S. aureus* resistance among all cultures, hospital wide *S. aureus* resistance among respiratory samples only, ICU-level *S. aureus* resistance among all cultures, ICU-level *S. aureus* resistance among respiratory samples, ICU-level GNR resistance among all cultures, and ICU-level GNR resistance among respiratory samples. Last, we developed yearly antibiograms for each facility between 2011 and 2014 to determine the hypothetical recommended use of broad spectrum antibiotics for each HAP patient based upon the ATS/IDSA provided thresholds.

Statistical Analysis

To assess the ATS/IDSA guidelines' ability to accurately identify patients at risk for resistant pathogens, we examined the alignment between the recommendation for broad-spectrum antimicrobials and the recovery of relevant pathogens. In our analysis we evaluated both the providers' behavior and the performance characteristics of the guidelines. We calculated provider sensitivity, defined as the proportion of admissions with positive cultures for MRSA or R-GNR that received an anti-MRSA drug or >1 anti-pseudomonal, and also the sensitivity of the guidelines, defined as the proportion of cultures positive for a resistant pathogen that would be recommended to receive broad spectrum treatment. Similarly, we calculated provider specificity (the proportion of admissions without a resistant infection on cultures that did not receive empiric treatment for resistance) and guideline specificity (those lacking positive cultures that would not be recommended to receive treatment for resistance by the guidelines). We calculated the potential overtreatment and undertreatment of those with HAP if guideline recommendations were followed. Potential overtreatment was defined as the proportion of all patients who had negative cultures but were treated. Potential undertreatment was defined as the proportion of all patients who had positive cultures but were not treated. We then completed both a univariable and multivariable regression analysis to determine the predictive ability of the provided thresholds and patient characteristics thought to confer increased risk of resistance for HAP. Patient characteristics included: IV antibiotics in the previous 90 days, mechanical ventilation in the 48 hours prior to admission, and pressor order.(4-6, 17, 18)

In our sensitivity analysis among all patients with a secondary diagnosis of pneumonia who did receive antibiotics or cultures in the initial 48 hours, we measured the rate of MRSA and R-GNR detection and estimated the empiric use of broad spectrum antibiotics if guideline recommendations were followed.

All statistical analyses were performed using STATA, Version 12.0 (StataCorp, College Station, TX) and R (http://cran.r-project.org). The study was conducted with approval from the University of Utah Institutional Review Board and the Salt Lake City VA Human Research Protection Program.

RESULTS:

Patient characteristics, antimicrobial coverage, and culture and detection

Of a total of 1.8 million hospitalizations at 113 facilities over three years, 76,227 (4.23%) hospitalizations had a secondary diagnosis of pneumonia. After exclusion of those admitted for respiratory distress or sepsis, and subsequently those who received antibiotics or cultures in the first 48 hours of admission, the remaining 3,562 (0.20%) met our criteria for HAP leading to an incidence rate of 3.7 HAPs per 10,000 hospital days in patients without initial infection on admission. Manual chart review (conducted by AB) to validate the precision of our definition of HAP patients found a positive predictive value of 92.00%. Among the 3,562 hospitalizations, median patient age was 69 years (mean 71, interquartile range 64-79), and median length of stay was 16 days (mean 22 days, interquartile range 10-26 days). Two-thousand, six-hundred and seventy-six (75.13%) of the admissions were to a medical service and 885 (24.85%) were to a surgical service. See Table 1 for associated comorbidities. Seven-hundred and sixty-four (21.45%) patients spent at least one day in the intensive care unit (ICU) during their admission, 72 patients

(2.02%) had an order for vasopressors, and 94 patients (2.64%) received mechanical ventilation in the 48 hours prior to the HAP episode. Five-hundred and seventy-nine (16.25%) patients died within 30 days of their admission. Regarding cultures: 3,042 (85.40%) had blood cultures, 1,761 (49.44%) had respiratory cultures, and 1,447 (40.62%) had both. Of those patients mechanically ventilated, 778 (82.98%) had respiratory cultures obtained. MRSA was detected by culture in 184 patients (5.17%) and R-GNR were detected in 82 patients (2.30%) despite positive blood or respiratory cultures in 1,199 (33.66%) patients. (Table 1) The most common pathogens identified were *S. aureus*, *P. aeruginosa* and Klebsiella. (Table E1)

Antibiogram Feasibility and Utility

Among 113 VAMCs, we found 84 (74.34%) could generate annual, facility wide, *Staphylococcus aureus* methicillin antibiograms from all hospital cultures according to Clinical and Laboratory Standards Institute guidelines.(16) However, only 16 (14.16%) could generate antibiograms for MRSA from respiratory samples. For the ICUs, 17 (15.04%) could generate MRSA antibiograms and 68 (60.18%) could generate GNR antibiograms from all cultures though when limited to respiratory cultures only 2 (1.77%) could generate antibiograms for MRSA and 14 (12.39%) for GNR resistance. When evaluating the prevalence of resistance between 2014 and 2017 among all centers we found the median facility-level prevalence of MRSA was 49% (interquartile range=44-54%) and the median R-GNR prevalence was 6.7% (interquartile range=4.3-9.3%). Almost all VAMCs (112, 99.12%) had a prevalence of MRSA greater than 20%. For resistant GNR, the

prevalence among ICU's was much more varied though the majority had a prevalence of resistance to piperacillin-tazobactam less than 20% (Figure 2).

Predictive performance of ATS/IDSA thresholds and patient characteristics for resistant infection

Among patients with HAP, 2,010 (56.43%) were empirically treated for MRSA and 809 (22.71%) were empirically treated for R-GNR with two or more anti-pseudomonals. The sensitivity and specificity of the clinician's empiric MRSA treatment was 69% (95% confidence interval [CI], 61.47 – 75.94%) and 39% (95% CI, 37.32 – 40.78%) respectively. For R-GNR, the sensitivity and specificity of clinicians' empiric treatment was 38% (95% CI, 26.36 – 49.70%) and 76% (95% CI, 74.04 – 77.04%) respectively. Using the ATS/IDSA specified threshold, we found that 3,561 (99.97%) of HAP patients were admitted to facilities with >20% prevalence of resistance so that all but one patient would be recommended to have coverage for MRSA by the guidelines, though only 184 patients (5.17%) grew MRSA on relevant cultures. The sensitivity of this treatment threshold was 100% (95% CI, 98.02% - 100.00%) and the specificity was 0.03% (95% CI, 0.00% - 0.16%). This indicates that 94.81% (95% CI, 94.02 - 95.50%) of patients would be potentially overtreated using the 20% threshold for empiric coverage and no patients would be undertreated for MRSA. When incorporating the ATS/IDSA patients characteristics including intravenous antibiotics within the past 90 days, shock and ventilator requirement at time of HAP all patients but one would be recommended to receive empiric MRSA coverage, and 778 (21.84%) patients would be recommended to have R-GNR coverage with 2 anti-pseudomonal agents. By univariable and multivariable analysis we did not find a MRSA prevalence of ≥ 20% or mechanical ventilation to

be significantly associated with an increased rate of MRSA detection (threshold $p<0.05$). We did find orders for vasopressors (odds ratio [OR], 3.89; 95% CI, 1.17 – 12.91, $p = 0.03$) and IV antibiotics in the last 90 days (OR, 1.98; 95% CI, 1.03 - 3.81, $p = 0.04$) to be associated with an increased risk of MRSA detection. For R-GNR we did not find an association between increased risk of resistant infection and IV antibiotics in the last 90 days or vasopressor order. However, we did find mechanical ventilation to be associated with increased risk of culture-proven R-GNR infection (OR 4.37; 95% CI, 1.52-12.57, $p = 0.01$). (Table 2)

Sensitivity Analysis

Among all patients with a secondary pneumonia without a principal diagnosis of respiratory distress or sepsis (31,560 patients), we found 27,024 (85.63%) were admitted to a medical service, 4,500 (14.26%) were admitted to a surgical service, and 36 patients (0.11%) were admitted to non-medical and non-surgical services. Six-hundred and six patients (1.92%) grew MRSA on relevant cultures and 272 patients (0.86%) grew R-GNR. The most common pathogens identified were *S. aureus*, *P. aeruginosa* and *Klebsiella spp*. (Table E2) Using the ATS/IDSA specified threshold for anti-MRSA therapy, we found that 31,516 patients (99.86%) would be recommended to receive anti-MRSA treatment. When including those who had received antibiotics in the past 90 days this increased the number indicated to have anti-MRSA therapy to 31,520 (99.87%). Additionally, when evaluating the number of patients recommended to receive dual anti-pseudomonal therapy from our larger cohort, we found that 23,724 (75.17%) received antibiotics on admission which would lead to the recommendation for dual anti-pseudomonals at time of HAP. Furthermore, when incorporating patients characteristics including shock and

ventilator requirement at time of HAP an additional 139 patients would be recommend to receive dual anti-pseudomonal therapy indicating that a total of 23,863 (75.61%) would be recommended to have dual anti-pseudomonal coverage.

DISCUSSION:

Our study is the first to examine the potential consequences of the ATS/IDSA guidelines using resistance prevalence thresholds to help guide antimicrobial decisions and their performance as tools to identify resistant infections in a large multicenter study. We found the number of patients treated with antibiotics against MDR pathogens far exceeded the number of cultures found to display antibiotic resistance. Additionally, when applying the guideline-recommended prevalence of resistance thresholds at which broad-spectrum coverage should be initiated, we found this would substantially increase the use of anti-MRSA antimicrobials compared to clinical practice without improved predictive performance had the guidelines been in place historically. The reason for this is likely multifactorial. It may in part be due to the inherent difficulty in a universal threshold when there is overall low prevalence of resistant infection. Additionally, this finding may emphasize that the risk of infection with a resistant pathogen is more dependent on the particular pathogen in concert with a susceptible host. Factors influencing host susceptibility may include underlying lung disease, history or resistant infection, history of antimicrobial use and ventilator associated injury.

The rate of detection of resistant organisms in our population is similar to rates found in the VA system in HCAP albeit lower than that described by Chung et al. in their cohort from Asia, though the most common pathogens were similar.(19, 20) Our rates of resistance were more consistent with those found by Kollef et al.

potentially due to more similar populations, severity of illness and sampling practices.(21) Our findings are in concert with Ekren et al. who also found very high sensitivity for the given resistant risk factors and very poor specificity leading to significant potential overtreatment.(22) Additionally, the risk factors we found to be significantly associated with resistant infection were consistent with the findings of Martin-Loeches et al (i.e., including IV antibiotics in the past 90 days, shock and mechanical ventilation). (23)

Our study has several limitations. We used administrative data that relied upon principal diagnostic codes to identify cases of pneumonia and therefore may not have captured all HAPs due to inconsistent diagnostic coding practices or missed diagnosis. Additionally, our detection rates of resistant infection were limited by the culturing practices of the providers. While overall there was a high rate of blood cultures, respiratory cultures were obtained in only about half of admissions. A larger percentage of patients mechanically ventilated had respiratory cultures obtained though overall the number mechanically ventilated in the 48 hours prior to their infection was small (2.64%). We defined Gram-negative resistance as resistance to piperacillin-tazobactam for purposes of feasibility, because it is a common treatment for HAP and a primary agent recommend by the ATS/IDSA for HAP. Additionally, it is the most common anti-pseudomonal that was administered for CAP across the VA after fluoroquinolones.(8) However, because hospitals may have different antimicrobial practices this may limit the generalizability of our results. Our primary analysis was limited to patients who were admitted to the hospital without receipt of antibiotics or cultures upon admission in order to ensure that we captured new diagnoses of pneumonia (rather than a late diagnosis of community acquired pneumonia) and no additional infectious diseases that could

complicate the antibiotic choices. As this approach substantially reduced our sample size and potentially skewed our population to a healthier subset of patients, this limits the generalizability of our findings. However, we also completed a sensitivity analysis of all patients with secondary diagnosis of pneumonia, including those who received antibiotics and cultures within the first 48 hours. This cohort demonstrated lower rates of detected resistance, but suggested similar consequences of guidelines on treatment: all members would be recommended to receive anti-MRSA therapy and 75% would be recommended to receive dual anti-pseudomonals given the guideline recommendations. Furthermore, given that the facility-level prevalence of MRSA in *S. aureus* antibiograms was >20% in almost all facilities over the time period evaluated, nearly universal anti-MRSA coverage would be recommended for HAP regardless of admission type. Therefore, despite the restricted nature of our primary HAP cohort our study suggests that antibiogram-guided therapy at the recommended thresholds would substantially increase unnecessary broad-spectrum antibiotic use for HAP in more generalized patient populations. Last, our study included secondary diagnoses of pneumonia, not only culture-confirmed cases. Because of this, we likely included patients who lacked true infection. Unfortunately, this is the clinical reality of pneumonia: there is no gold standard for the diagnosis of pneumonia and cultures are rarely revealing. Our chart review did, however, demonstrate a relatively high positive predictive value in our cohort of interest.

Recommendations for the optimal empiric treatment of HAP must balance the need for effective patient treatment while minimizing unwarranted broad-spectrum antibiotic use. In order to achieve this, previous guidelines have emphasized limiting broad-spectrum use to those with either increased risk for resistant

infection due to patient characteristics or the patient's environmental exposure to resistant pathogens. At present, the evidence behind using a single antibiogram-based threshold to guide broad-spectrum antibiotic use is limited, making universal recommendations difficult. Focusing on refining our understanding of host susceptibility and host-pathogen interactions (and thus on patient-specific rather than population-level risk of infection by resistant pathogens), while working to establish improved rapid diagnostic testing and resistance prediction are the most promising pathways for adequate empiric treatment. In the meantime, clinicians and stewardship programs will be wise to heed the guideline's admonition to use local data to anticipate potential impact and inform local adaptation of guideline implementation. Future research evaluating the comparative benefits and harms of initial broad spectrum treatment will be instrumental to evaluating the risk associated with different empiric strategies.

Figure 1. Study population

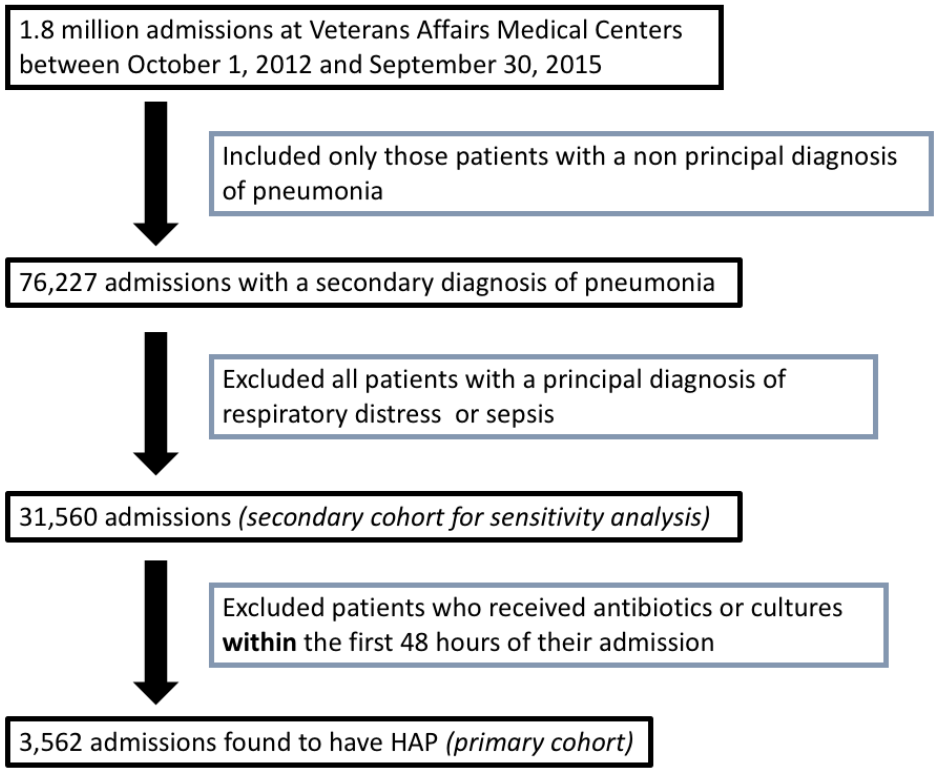

Table 1. Demographics and clinical characteristics of patients

Demographics and clinical characteristics of HAP patients	
	N = 3,562 patients
Demographic	
Age – median (IQR)	69 yr (64-79)
Male sex – N (%)	3,487 (97.89%)
Clinical	
LOS – median (IQR)	22 days (10-26)
Admitted to Medical Service – N (%)	2,676 (75.13%)
Admitted to Surgical Service – N (%)	885 (24.85%)
Renal disease – N (%)	430 (12.07%)
Heart failure – N (%)	587 (16.48%)
Cerebrovascular disease– N (%)	428 (12.02%)
Diabetes mellitus – N (%)	977 (27.43%)
Cancer – N (%)	662 (18.39%)
IV antibiotics in 90 days – N (%)	639 (17.94%)
ICU admission – N (%)	764 (21.45%)
Pressor order – N (%)	72 (2.00%)
Mechanical ventilation – N (%)	94 (2.64%)
30 day mortality – N (%)	579 (16.25%)
Antibiotics	
MRSA coverage – N (%)	2,010 (56.43%)
No anti-pseudomonal – N (%)	720 (20.21%)
1 anti-pseudomonal – N (%)	1743 (48.93%)
≥ 2 anti-pseudomonals –N (%)	809 (22.71%)
Cultures	
Blood – N (%)	3,042 (85.40%)
Respiratory – N (%)	1,761 (49.44%)
Blood and respiratory –N (%)	1,447 (40.62%)
Positive blood or respiratory culture – N (%)	1,199 (33.66%)
MRSA positive – N (%)	184 (5.17%)
R-GNR positive – N (%)	82 (2.30%)

Figure 2. Prevalence of resistance in antibiograms at 113 VAMCs from all hospital cultures

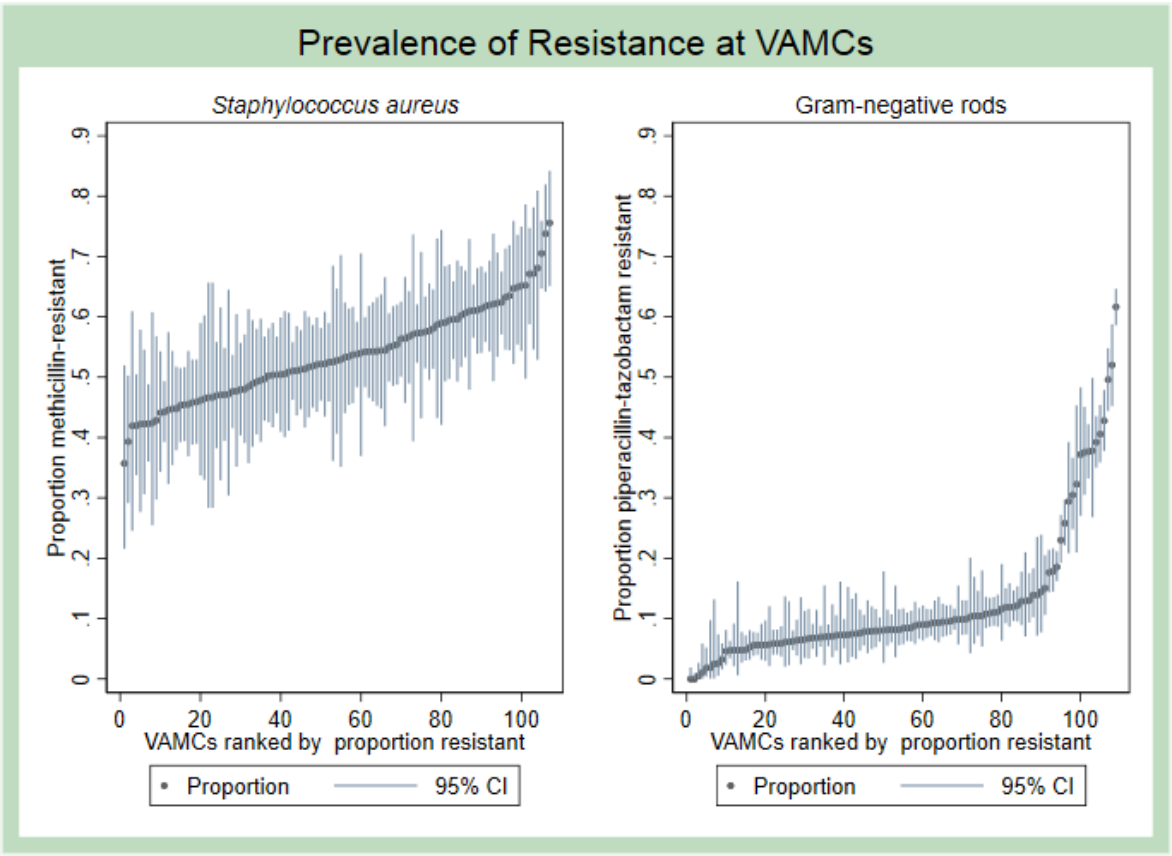

Table 2. Multivariable Model for Resistant Infection

Multivariable Model for Resistant Infection in HAP

Variables for MRSA resistance	Odds Ratio (95% CI)	P Value
20% threshold	undefined*	*
IV antibiotics in last 90 days	1.98 (1.03 – 3.81)	0.04
Pressor order	3.89 (1.17 – 12.91)	0.03
Mechanical ventilation	1.82 (0.43 – 7.67)	0.41
	AUC = 0.55	
Variables for GNR resistance		
IV antibiotics in last 90 days	1.00 (0.44 – 2.28)	0.99
Pressor order	1.33 (0.18 – 9.86)	0.78
Mechanical ventilation	4.37 (1.52 – 12.57)	0.01
	AUC = 0.55	

* The odds ratio is undefined as no patients were in facilities where the prevalence of resistance was ≤ 20% therefore the denominator was 0.

438

439

440Table E1.

Organisms Recovered from 3,562 Patients with HAP			
Organism	**Sample Type**	**Number of positive cultures**	**Proportion Resistant**
Staphylococcus aureus	sputum	323	0.45
Pseudomonas aeruginosa	sputum	184	0.11
Genus Klebsiella	sputum	154	0.14
Escherichia coli	sputum	106	0.06
Staphylococcus aureus	blood	100	0.45
Genus Enterobacter	sputum	80	0.24
Genus Serratia	sputum	40	0.15
Genus Klebsiella	blood	38	0.05
Escherichia coli	blood	37	0.03
Genus Stenotrophomonas	sputum	32	0
Genus Proteus	sputum	31	0
Genus Citrobacter	sputum	21	0.05
Genus Acinetobacter	sputum	12	0
Genus Enterobacter	blood	12	0.25
Pseudomonas aeruginosa	blood	12	0.25
Genus Proteus	blood	<10	0
Genus Serratia	blood	<10	0
Genus Stenotrophomonas	blood	<10	0
Genus Acinetobacter	blood	<10	0.2
Genus Citrobacter	blood	<10	0
Genus Morganella	sputum	<10	0
Raoultella planticola	sputum	<10	0
Pantoea agglomerans	sputum	<10	0.5
Raoultella ornithinolytica	sputum	<10	0
Genus Providencia	sputum	<10	0
Hafnia alvei	sputum	<10	1
Family Enterobacteriaceae	sputum	<10	0

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442Table E2.

Organisms Recovered from 31,560 Patients with Secondary Pneumonia			
Organism	**Sample Type**	**Number of positive cultures**	**Proportion Resistan**

Staphylococcus aureus	sputum	960	0.54
Pseudomonas aeruginosa	sputum	646	0.11
Genus Klebsiella	sputum	475	0.16
Escherichia coli	sputum	304	0.13
Genus Enterobacter	sputum	244	0.26
Staphylococcus aureus	blood	198	0.48
Genus Stenotrophomonas	sputum	145	0.02
Genus Serratia	sputum	132	0.10
Genus Klebsiella	blood	97	0.15
Genus Proteus	sputum	83	0.02
Escherichia coli	blood	82	0.04
Genus Citrobacter	sputum	64	0.11
Genus Acinetobacter	sputum	63	0.11
Pseudomonas aeruginosa	blood	45	0.09
Genus Enterobacter	blood	30	0.27
Genus Serratia	blood	18	0.00
Genus Proteus	blood	14	0.00
Genus Acinetobacter	blood	12	0.08
Genus Providencia	sputum	12	0.42
Genus Morganella	sputum	11	0.00
Genus Stenotrophomonas	blood	<10	0.00
Genus Citrobacter	blood	<10	0.17
Raoultella planticola	sputum	<10	0.00
Hafnia alvei	sputum	<10	0.20
Pantoea agglomerans	sputum	<10	0.33
Genus Providencia	blood	<10	0.33
Genus Morganella	blood	<10	0.00
Family Enterobacteriaceae	sputum	<10	0.00
Cronobacter sakazakii	sputum	<10	0.00
Kluyvera species	sputum	<10	0.00
Raoultella ornithinolytica	sputum	<10	0.00
Pantoea species	blood	<10	0.00
Pantoea species	sputum	<10	0.00
Yokenella regensburgei	sputum	<10	0.00
Leclercia adecarboxylata	sputum	<10	0.00

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